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The role of oxidative stress in degeneration of the neuromuscular junction in amyotrophic lateral sclerosis

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Abstract

Amyotrophic lateral sclerosis (ALS) is characterized by the progressive loss of motoneurons and degradation of the neuromuscular junctions (NMJ). Consistent with the dying-back hypothesis of motoneuron degeneration the decline in synaptic function initiates from the presynaptic terminals in ALS. Oxidative stress is a major contributory factor to ALS pathology and affects the presynaptic transmitter releasing machinery. Indeed, in ALS mouse models nerve terminals are sensitive to reactive oxygen species (ROS) suggesting that oxidative stress, along with compromised mitochondria and increased intracellular Ca2+ amplifies the presynaptic decline in NMJ. This initial dysfunction is followed by a neurodegeneration induced by inflammatory agents and loss of trophic support. To develop effective therapeutic approaches against ALS, it is important to identify the mechanisms underlying the initial pathological events. Given the role of oxidative stress in ALS, targeted antioxidant treatments could be a promising therapeutic approach. However, the complex nature of ALS and failure of monotherapies suggest that an antioxidant therapy should be accompanied by anti-inflammatory interventions to enhance the restoration of the redox balance. © 2014 Pollari, Goldsteins, Bart, Koistinaho and Giniatullin.

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Keywords

ALS, Neurodegeneration, Neuromuscular junction, Oxidative stress, ROS